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INFORMATION DISCLOSURE  
IN AN APPLICATION

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Sheet

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OF

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Docket Number  
103576.166

Application Number  
09/460,293

Applicant  
Chen, Zhijian H.

Filing Date

September 24, 1999

Group Art Unit

1652

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U.S. Patent Documents						
EXAMINER INITIAL	DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE

Foreign Patent Documents						
EXAMINER INITIAL	DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION YES NO

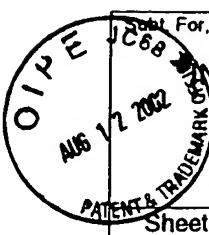
Other Documents (Including Author, Title, Date Pertinent Pages, Etc.)

A1	Alkalay, et al., "In Vitro Stimulation of IκB Phosphorylation Is Not Sufficient to Activate NF-κB", <i>Mol. Cell. Biol.</i> , Vol. 15, No. 3, pp. 1294-1304 (1995)
A2	Alkalay, et al., "Stimulation-Dependent IκB-α Phosphorylation Marks the NF-κB inhibitor for Degradation via the Ubiquitin-Proteasome Pathway" <i>Proc. Natl. Acad. Sci. USA</i> , Vol. 92, pp. 10599-10603 (1995)
A3	Arnason and Ellison, "Stress Resistance in <i>Saccharomyces cerevisiae</i> Is Strongly Correlated with Assembly of a Novel Type of Multiubiquitin Chain" <i>Mol. Cell. Biol.</i> , Vol. 14, No. 12, pp. 7876-7883 (1994)
A4	Auffray, et al., "IMAGE: Integrated Molecular Analysis of the Human Genome and Its Expression" <i>Science</i> , Vol. 318, pp. 263-272 (1995)
A5	Auphan et al., "Immunosuppression by Glucocorticoids: Inhibition of NF-κB Activity Through Induction of IκB Synthesis" <i>Science</i> , Vol. 270, pp. 286-290 (1995)
A6	Baeuerle and Henkel, "Function and Activation of NF-κB in the Immune System" <i>Annu. Rev. Immunol.</i> , Vol. 12, pp. 141-179 (1994)
A7	Baldi, et al., "Critical Role for Lysines 21 and 22 in Signal-Induced, Ubiquitin-Mediated Proteolysis of IκB-α" <i>J. Biol. Chem.</i> , Vol. 271, No. 1, pp. 376-379 (1996)
A8	Barroga et al., "Constitutive Phosphorylation of IκB-α by Casein Kinase II" <i>Proc. Natl. Acad. Sci.</i> , Vol. 92, pp. 7637-7641 (1995)
A9	Beg, et al., "Tumor Necrosis Factor and Interleukin-1 Lead to Phosphorylation and Loss of IκB-α: a Mechanism for NF-κB Activation." <i>Mol. Cell. Biol.</i> , pp. 3301-3310 (1993) 176
A10	Belvin, et al., "Cactus Protein Degradation Mediates Drosophila Dorsal-Ventral Signaling" <i>Genes and Dev.</i> , Vol. 9, pp. 783-793 (1995)
A11	Blank, et al., "Molecular Cloning of Mitogen-activated Protein/ERK Kinase Kinases (MEKK) 2 and 3" <i>J. Biol. Chem.</i> , Vol. 271, No. 10, pp. 5361-5368 (1996)
A12	Brockman, J.A., "Coupling of a Signal Response Domain in IκB-α to Multiple Pathways for NF-κB Activation" <i>Mol. Cell. Biol.</i> , Vol. 15, No. 5 (1995) 2809-2818
A13	Brown, et al., "Control of IκB-α Proteolysis by Site-Specific, Signal-Induced Phosphorylation" <i>Science</i> , Vol. 267, pp. 1485-1488 (1995)
A14	Chau, "A Multiubiquitin Chain is Confined to Specific Lysine in a Targeted Short-Lived Protein" <i>Science</i> , Vol. 243, pp. 1576-1583 (1989)

EXAMINER	DATE CONSIDERED
<i>CP Mallon</i>	<i>3/11/03</i>

EXAMINER: Initial citation is considered, whether or not citation is in conformance with MPEP § 609. Draw Line through citation if not conformance and not considered. Include copy with next communication to applicant.

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INFORMATION DISCLOSURE IN AN APPLICATION <i>(Use several sheets if necessary)</i>				Docket Number 103576.166	Application Number 09/460,293 10/052,003
				Applicant Chen, Zhijian H.	RECEIVED AUG 14 2002
				Filing Date September 24, 1999	Group Art Unit 1652 TECH CENTER 1600/2
Sheet	2	OF	5		

B1	Chen, et al., "Multiple Ubiquitin-Conjugating Enzymes Participate in the In Vivo Degradation of the Yeast MATα2 Repressor" <i>Cell</i> , Vol. 74, pp. 357-369 (1993)
B2	Chen, et al., "Signal-Induced Site-Specific Phosphorylation Targets IκB-α to the Ubiquitin-Proteasome Pathway" <i>Genes and Dev.</i> , Vol. 9, pp. 1586-1597 (1995)
B3	Chen, et al., "Site-Specific Phosphorylation of IκB-α by a Novel Ubiquitination-Dependent Protein Kinase Activity" <i>Cell</i> , Vol. 84, (1996) (957-862)
B4	Chen and Pickart, "A 25-Kilodalton Ubiquitin Carrier Protein (E2) Catalyzes Multi-ubiquitin Chain Synthesis via Lysine 48 of Ubiquitin" <i>J. Biol. Chem.</i> , Vol. 265, No. 35, pp. 21835-21842 (1990)
B5	Choi, et al., "Ste5 Tethers Multiple Protein Kinases in the MAP Kinase Cascade Required for Mating in <i>S. cerevisiae</i> " <i>Cell</i> , Vol. 78, pp. 499-512 (1994)
B6	Ciechanover, "The Ubiquitin-Proteasome Proteolytic Pathway" <i>Cell</i> , Vol. 79, pp. 13-21 (1994)
B7	Derijard, et al., "Independent Human MAP Kinase Signal Transduction Pathways Defined by MEK and MKK Isoforms" <i>Science</i> , Vol. 267, pp. 682-685 (1995)
B8	Derijard, et al., "JNK1: A Protein Kinase Stimulated by UV Light and Ha-Ras That Binds and Phosphorylates the c-Jun Activation Domain" <i>Cell</i> , Vol. 76, pp. 1025-1037 (1994)
B9	Devary, et al., "NF-κB Activation by Ultraviolet Light Not Dependent on a Nuclear Signal" <i>Science</i> , Vol. 261, pp. 1442-1445 (1993)
B10	Diaz-Meco, "PKC Induces Phosphorylation and Inactivation of I kappa B-alpha In Vitro" <i>EMBO J.</i> , Vol 13, No. 12, pp. 2842-2848 (1994)
B11	DiDonato, et al., "Phosphorylation of IκBα Precedes but IS Not Sufficient for Its Dissociation from NF-κB" <i>Mol. Cell. Biol.</i> , Vol. 15, No. 3, pp. 1302-1311 (1995)
B12	Dominguez, et al., "Inhibition of Protein Kinase C ζ Subspecies Blocks the Activation of an NF-κB-like activity in Xenopus Laevis Oocytes" <i>Mol. Cell. Biol.</i> , Vol. 13, No. 2, pp. 1290-1295 (1993)
B13	Finco, et al., "Inducible phosphorylation of IκBα is not sufficient for its dissociation from NF-κB and is inhibited by protease inhibitors" <i>Proc. Natl. Acad. Sci. USA</i> , Vol. 91, pp. 11884-11888 (1994)
B14	Finco and Baldwin, "κB Site-Dependent Induction of Gene Expression by Diverse Inducers of Nuclear Factor κB Requires Raf-1", <i>J. Biol. Chem.</i> , Vol. 268, No. 24, pp. 17676-17679 (1993)
B15	Finco and Baldwin, "Mechanistic Aspect of NF-κB Regulation: The Emerging Role of Phosphorylation and Proteolysis" <i>Immunity</i> , Vol. 3, pp. 263-272 (1995)
B16	Francis and Corbin, "Structure and Function of Cyclic Nucleotide-dependent Protein Kinases" <i>Annu. Rev. Physiol.</i> , Vol. 56, pp. 237-72 (1994)
B17	Ghosh and Baltimore, "Activation Invitro of NF-κB by Phosphorylation of its Inhibitor IκB" <i>Nature</i> , Vol. 344, pp. 678-682 (1990)
B18	Goldberg, Alfred L., "Functions of the Proteasome: The Lysis at the End of the Tunnel" <i>Science</i> , Vol. 268, pp. 522-523 (1995)

EXAMINER <i>C. Mallon</i>	DATE CONSIDERED <i>9/6/03</i>
EXAMINER: Initial if citation is considered, whether or not citation is in conformance with MPEP § 609: Draw Line through citation if not conformance and not considered. Include copy with next communication to applicant.	

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Sub For, PTO-1449				Docket Number 103576.166	Application Number 00/460,293
INFORMATION DISCLOSURE IN AN APPLICATION <i>(Use several sheets if necessary)</i>				Applicant Chen, Zhijian H.	10/05/2002
Sheet	3	OF	5	Filing Date September 24, 1999	Group Art Unit 1652

C1	Gupta, et al., "Transcription Factor ATF2 Regulation by the JNK Signal Transduction Pathway" <i>Science</i> , Vol. 267, pp. 389-393 (1995)
C2	Haskill, et al., "Characterization of an Immediate-Early Gene Induced in Adherent Monocytes that Encodes IκB-like Activity" <i>Cell</i> , Vol. 65, pp. 1281-1289 (1991)
C3	Henkel, et al., "Rapid Proteolysis of IκB-α is Necessary for Activation of Transcription Factor NF-κB" <i>Nature</i> , Vol. 365, pp. 182-185 (1993)
C4	Hershko and Heller, "Occurrence of a Polyubiquitin Structure in Ubiquitin-Protein Conjugates" <i>Biochem. Biophys. Res. Commun.</i> , Vol. 128, No. 3, pp. 1079-1086 (1985)
C5	Hershko and Ciechanover, "The Ubiquitin System for Protein Degradation" <i>Annu. Rev. Biochem.</i> , Vol. 61, pp. 761-807 (1992)
C6	Hibi, et al., "Identification of an oncoprotein- and UV-responsive protein kinase that binds and potentiates the c-Jun activation domain" <i>Genes and Dev.</i> , Vol. 7, pp. 2135-2148 (1993)
C7	Higgins, et al., "Antisense inhibition of the p65 subunit of NF-κB blocks tumorigenicity and causes tumor regression" <i>Proc. Natl. Acad. Sci. USA</i> , Vol. 90, pp. 9901-9905 (1993)
C8	Hirano, et al., "MEK-Kinase Is Involved in Tumor Necrosis Factor α-Induced NF-κB Activation and Degradation of IκB-α" <i>J. Biol. Chem.</i> , Vol. 271, No. 22, pp. 13234-13238 (1996)
C9	Kumar, A., et al., "Double-Stranded RNA-Dependent Protein Kinase Activates Transcription Factor NF-κB by Phosphorylating IκB" <i>Proc. Natl. Acad. Sci. USA</i> Vol. 91, pp. 6288-6292 (1994)
C10	Kuno, et al., "Identification of an IκB-α - Associated Protein Kinase in a Human Monocytic Cell Line and Determination of its Phosphorylation Sites on IκB-α" <i>Biol. Chem.</i> Vol. 270, No. 46, pp. 27914-27919 (1995)
C11	Lange-Carter, et al., "A Divergence in the MAP Kinase Regulatory Network Defined by MEK Kinase and Raf" <i>Science</i> , Vol. 260, pp. 315-319 (1993)
C12	Li and Sedivy "Raf-1 Protein Kinase Activates the NF-κB Transcription Factor By Disassociating the Cytoplasmic NF-κB-IκB complex" <i>Proc Natl Acad Sci USA.</i> , Vol. 90, pp. 9247-9251 (1993)
C13	Lin, et al., "Activation of NF-κB requires proteolysis of the inhibitor IκB-α: Signal-induced phosphorylation of IκB-α alone does not release active NF-κB" <i>Proc. Natl. Acad. Sci. USA</i> , Vol. 92, pp. 552-556, (1995)
C14	Lin and Desiderio, "Regulation of V(D)J Recombination Activator Protein RAG-2 by Phosphorylation" <i>Science</i> , Vol. 260, pp. 953-959 (1993)
C15	Mellits, et al., "Proteolytic degradation of MAD3 (IκBα) and enhanced processing of the NF-κB precursor p105 are obligatory steps in the activation of NF-κB" <i>Nucl. Acid. Res.</i> , Vol. 21, No. 22, pp. 5059-5066 (1993)
C16	Miyamoto, et al., "Tumor necrosis factor α-induced phosphorylation of IκBα is a signal for its degradation but not dissociation from NF-κB" <i>Proc. Natl. Acad. Sci. USA</i> , Vol. 91, pp. 12740-12744 (1994)

EXAMINER: <i>[Signature]</i>	DATE CONSIDERED 3/6/03
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Subj. For, PTO-1449				Docket Number 103576.166	Application Number 09/460,293 10/052,605 1 2002
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Sheet .	4	OF	5	Filing Date September 24, 1999	Group Art Unit 1652

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D1	Nishizawa, M., et al., "Degradation of MOS by the N-terminal Proline (Pro2)-Dependent Ubiquitin Pathway on Fertilization of Xenopus Eggs: Possible Significance of Natural Selection for Pro2 in MOS" <i>EMBO J.</i> , Vol. 12, No. 10, pp. 4021-4027 (1993)
D2	Palombella , et al., "The Ubiquitin-Proteasome Pathway is Required For Processing the NF- $\kappa$ B1 Precursor Protein and the Activation of NF- $\kappa$ B" <i>Cell</i> , Vol. 78, pp. 773-785 (1994)
D3	Pawlak, et al., "Characterization of a Large Population of mRNAs From Human Testis" <i>Genomics</i> , Vol. 26, pp. 151-158 (1995)
D4	Pickart and Rose, " Functional Heterogeneity of Ubiquitin Carrier Proteins" <i>J. Biol. Chem.</i> , Vol. 260, No. 3, pp. 1573-1581 (1985)
D5	Read, et al., "The Proteasome Pathway Is Required for Cytokine-Induced Endothelial-Leukocyte Adhesion Molecule Expression" <i>Immunity</i> , Vol. 2, pp. 493-506 (1995)
D6	Rodriguez, M.S., et al, "Inducible Degradation of I $\kappa$ B $\alpha$ In Vitro and In Vivo Requires the Acidic C-Terminal Domain of the Protein" <i>Mol. Cell. Biol.</i> , Vol. 15(5), pp. 2413-2419 (1995)
D7	Scherer, et al., "Signal-Induced Degradation of I $\kappa$ B- $\alpha$ requires site-specific Ubiquitination" <i>Natl. Acad. Sci. USA.</i> , Vol. 92, pp. 11259-11263 (1995)
D8	Schreck, et al., "Reactive Oxygen Intermediates as Apparently Widely Used Messengers in the Activation of the NF- $\kappa$ B Transcription Factor and HIV-1" <i>EMBO J.</i> , Vol. 10 No. 8, pp. 2247-2258 (1991)
D9	Schutze, et al., "TNF Activates NF-kappa B by Phosphatidylcholine-Specific Phospholipase C-Induced "Acidic" Sphingomyelin Breakdown" <i>Cell</i> , Vol. 71 pp.765 -777
D10	Siebenlist, et al., "Structure, Regulation and Function of NF- $\kappa$ B" <i>Annu. Rev. Cell Biol.</i> , Vol. 10, pp. 405-455 (1994)
D11	Sun, et al., " NF- $\kappa$ B Controls Expression of Inhibitor I $\kappa$ B- $\alpha$ : Evidence For An Inducible Autoregulatory Pathway", <i>Science</i> , Vol. 259, pp. 1912-1915 (1993)
D12	Thanos and Maniatis, "NF- $\kappa$ B: A Lesson in Family Values" <i>Cell</i> , Vol. 80, pp. 529-532 (1995)
D13	Thévenin, et al., "Induction of Nuclear Factor- $\kappa$ B and the Human Immunodeficiency Virus Long Terminal Repeat by Okadaic Acid, A Specific Inhibitor of Phosphatases 1 and 2A" <i>New Biol.</i> , Vol. 2, pp. 793-800 (1990)
D14	Traenckner et al., "A Proteasome Inhibitor Prevents Activation of KF- $\kappa$ B and Stabilizes a Newly Phosphorylated Form of I $\kappa$ B- $\alpha$ That is Still Bound to NF- $\kappa$ B" <i>EMBO J.</i> , Vol. 13, pp.5433-5441 (1994)
D15	Traenckner, E.B.-M.,et al, "Phosphorylation of Human I $\kappa$ B- $\alpha$ on Serines 32 and 36 Controls I $\kappa$ B- $\alpha$ Proteolysis and NF- $\kappa$ B Activation in Response to Diverse Stimuli" <i>EMBO J.</i> , Vol. 14, No. 12, pp. 2876-2883 (1995)
D16	Verma, et al., "Rel/NF- $\kappa$ B/I $\kappa$ B Family: Intimate Tales of Association and Disassociation" <i>Genes and Dev.</i> , Vol. 9 pp. 2723-2735 (1995)
D17	Wasserman, "A Conserved Signal Transduction Pathway Regulating the Activity of the Rel-Like Proteins Dorsal and NF- $\kappa$ B" <i>Mol. Biol. Cell.</i> , Vol. 4, pp. 767-771 (1993)

EXAMINER <i>Walker</i>	DATE CONSIDERED <i>3/6/03</i>
EXAMINER: Initial if citation is considered, whether or not citation is in conformance with MPEP § 609: Draw Line through citation if not conformance and not considered. Include copy with next communication to applicant.	

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Searched For, PTO-1449				Docket Number 103576.166	Application Number 09/460,293
INFORMATION DISCLOSURE IN AN APPLICATION <i>(Use several sheets if necessary)</i>				Applicant Chen, Zhijian H.	1605200
Sheet	5	OF	5	Filing Date September 24, 1999	Group Art Unit 1652

E1	Whiteside , et al., "N- and C- Terminal Sequences Control Degradation of MAD3/IkB- $\alpha$ in Response to Inducers of NF- $\kappa$ B Activity" <i>Mol. Cell. Biol.</i> , Vol. 15 , No. 10, pp. 5339-5345 (1995)
E2	Yaglom, et al., " p34Cdc28-Mediated Control of Cln3 Cyclin Degradation" <i>Mol. Cell. Biol.</i> , Vol. 15, No. 2, pp. 731-741 (1995)
E3	Yang, et al., "Deficient signaling in mice devoid of double-stranded RNA-dependent Protein kinase" <i>EMBO J.</i> , Vol. 14, No. 24, pp. 6095-6106 (1995)
E4	EMBL Database entry Hs369288, Accession Number N56369, from International Search Report, International Application No. PCT/US97/04195
E5	EMBL Database entry Hs2038, Accession Number T19203, from International Search Report, International Application No. PCT/US97/04195

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Substantive PTO-1449				Docket Number 103576.166	Application Number 097406-293 10/052,001
INFORMATION DISCLOSURE IN AN APPLICATION <i>(Use several sheets if necessary)</i>				Applicant Chen	
Sheet	1	OF	1	Filing Date September 24, 1999	Group Art Unit 1652

U.S. Patent Documents						
EXAMINER INITIAL	DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE
CP AB	5,972,674	10/26/99	Mercurio, et al.	435	194	
AB	6,258,579	7/10/01	Mercurio, et al.	435	194	
AB	6,268,194	7/31/01	Karin, et al.	435	194	
AB	6,242,253	6/5/01	Karin, et al.	435	325	

Foreign Patent Documents						
EXAMINER INITIAL	DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION
						YES NO
CP AB	98/08955 ✓	3/5/98	WO			
AB	98/37228 ✓	8/27/98	WO			

Other Documents (Including Author, Title, Date Pertinent Pages, Etc.)	
CP AB	Lee et al. "Activation of the IκBα Kinase Complex by MEKK1, a Kinase of the JNK Pathway" Cell, Vol. 88, pp. 213-222 (1997)

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